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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/729,822

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Ronald Berenson

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EXAMINER

BELYAVSKYI, MICHAEL A

ART UNIT

PAPER NUMBER

1644

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DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/729,822	<b>Applicant(s)</b> BERENSON ET AL.	
	<b>Examiner</b> Michail A. Belyavskyi	<b>Art Unit</b> 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3, 11 and 12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 11 and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/25/08 has been entered.

Claims 1-3, 11 and 12 are pending.

In view of the amendment, filed 11/01/07 the following rejections remain:

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-3, 11 and 12 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,352,694 or WO'03/067221 or WO 03/024989 for the same reasons set forth in the previous Office Action, mailed on 05/01/07.

Applicant's arguments, filed 02/27 /07 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) the combined references must teach or suggest all claimed limitation, (ii) the tree cited references are directed to a method for expanding T cells and nowhere do cited references teach a method for eliminating subpopulation of T cells from a population of T cell using high bead: cell ration; (iii) US Patent '694 only teaches the use of 3:1 beads:cell ratio to selectively expand T cells; (iv) WO' 221 and WO'989 do not mention whatsoever to use beads conjugated to anti-CD3 anti-CD29 antibodies to delete cells.

Contrary to Applicant's assertion it has been recently stated that KSR forecloses the argument that a specific teaching, suggestion, or motivation are required to support a finding of obviousness See Board decision ( see *KSR International Co v Teleflex Inc.*, 550U.S.-, 82 USPQ2d 1385, 2007).

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US Patent '694 teaches a method of selectively expansion of a specific subpopulation of T cells, comprising exposing a mixed population of T cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells is high, i.e. 3:1 and further expanding said cells by culturing said cells with said beads at the ratio of bead to cell 1:1 ( see entire document, Abstract and columns 9, 19 , 20 and 28 and in particular). US Patent '694 teaches that the optimal ratio of beads to cells has to be determined by skill in the art and can be from 1:9 to 9:1 ( see column 20 in particular). US Patent '694 teaches that exposing a mixed population of T cells to said beads, wherein the ratio of beads to cells is 3:1 would result in selective elimination of CD8<sup>+</sup> T cells which would die by apoptosis ( see column 30 and Example 15 in particular). US Patent '694 further teach that selective elimination of a subpopulation of T cells by inducing apoptosis would be useful for further expanding remaining T cells ( see column 51 in particular).

With regard to Applicant's comments that US Patent '694 does not teach a method of selectively eliminating a portion of antigen-specific memory T cells.

It is noted that US Patent' 694 teaches that the claimed method can be used to generate a essentially homogeneous subpopulation of CD4<sup>+</sup> T cells from the mixed population of T cell from an individual, by exposing said mixed population of T cell to anti-CD3 antibody -anti-CD28 antibody attached to the beads ( see columns 27 and 30 in particular). In other words, US Patent '694 disclosed that after exposure of the mixed population of T cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads only one subpopulation survived and expanded. It is the Examiner position that one skill in the art would immediately recognized that said selectively expansion of a specific subpopulation of T cells from the mixed population of T cells is the result of the selectively elimination of the other subpopulations. Moreover, it is the Examiner position that US Patent'694 clearly envision said elimination of antigen-specific T cells. On overlapping columns 50 a 51, US Patent '694 teach that said selective generation of a essentially homogeneous subpopulation of CD4<sup>+</sup> T cells is achieved by elimination of a subpopulation of CD8<sup>+</sup> T cells by apoptosis. Thus, even if US Patent '694 does not explicitly recited a method for eliminating at least a substantial portion of T, it would be an intrinsic property of the reference method of exposing said mixed population of T cell to anti-CD3 antibody -anti-CD28 antibody attached to the beads, since the reference and claimed method administered the same anti-CD3 antibody -anti-CD28 antibody attached to the beads to the same mixed population of T cells . Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Com. v. Electro Materials Corp. of America 202 USPQ 22 (DC SINY ); and In re Burckel 201 USPQ 67 (CCPA).

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WO' 221 teaches a method of selectively expansion of a specific subpopulation of T cells, comprising exposing a mixed population of T cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells is high, i.e. 10:1 and further expanding said cells by culturing said cells with said beads at the ratio of bead to cell 1:1 ( see entire document, Abstract and pages 24 and 25 and in particular). WO' 221 further teaches administering a composition comprising fludarabine or cyclophosphamide ( see page 8 in particular) WO' 221 teaches that exposing a mixed population of T cells to said beads, wherein the ratio of bead to cell is high would result in selective expanding only CD4<sup>+</sup> T cell ( see overlapping pages 46-47).

WO' 989 teaches a method of selectively expansion of a specific subpopulation of T cells, comprising exposing a mixed population of T cells to pro-apoptotic composition ( see overlapping pages 16 and 17 in particular). WO' 989 teaches the use of anti-CD3 antibody - anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells is high, i.e. 10:1 and further expanding said cells by culturing said cells with said beads at the ratio of bead to cell 1:1 ( see entire document, pages 26 and in particular). WO' 989 teaches that using this methodologies , i.e. exposure to high and then low beads:cell ratio, it is possible to selectively expand a selective subpopulation of T cells from the mixed T cell population ( see page 50 , 53 and 75 and Table 7 on page 82 in particular).

With regard to Applicant's comments that WO' 989 and WO' 221 do not teach a method of selectively eliminating a portion of antigen-specific memory T cells.

It is noted that both WO' 989 and WO' 221 teaches that the claimed method can be used to generate a essentially homogeneous subpopulation of CD4<sup>+</sup> T cells from the mixed population of T cell from an individual, by exposing said mixed population of T cell to anti-CD3 antibody - anti-CD28 antibody attached to the beads. In other words, both WO' 989 and WO' 221 disclosed that after exposure of the mixed population of T cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads only specific subpopulation survived and expanded. It is the Examiner position that one skill in the art would immediately recognized that said selectively expansion of a specific subpopulation of T cells from the mixed population of T cells is the result of the selectively elimination of the other subpopulations. Thus, even if WO' 989 or WO' 221 does not explicitly recited a method for eliminating at least a substantial portion of T, it would be an intrinsic property of the reference method of exposing said mixed population of T cell to anti-CD3 antibody -anti-CD28 antibody attached to the beads, since the reference and claimed method administered the same anti-CD3 antibody -anti-CD28 antibody attached to the beads to the same mixed population of T cells . Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Com. v. Electro Materials Corp. of America 202 USPQ 22 (DC SINY ); and In re Burckel 201 USPQ 67 (CCPA).

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It is noted that US Patent 6,352,694 or WO'03/067221 or WO 03/024989 does not explicitly recited a method for eliminating at least a substantial portion of T cells comprising exposing a population of cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells is 5:1 as recited in the instant claims, or wherein the remaining mixed population is expanded by further exposing the cells to the surface, wherein the ratio of the surface to cell is from about 1:1 to about 1;10.

It is noted however, that the claimed ration of 5:1 and further expanding the remaining mixed population by exposing the cells to the surface, wherein the ratio of the surface to cell is from about 1:1 to about 1;10 are an obvious variation of the recited in US Patent 6,352,694 or WO'03/067221 or WO 03/024989 ratio of beads to cells absent of a showing of unobvious property . Moreover, it would be conventional and within the skill of the art to identify and determine the optimum ratio of beads to cell to induce apoptosis or growth inhibition. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Claims 11 and 12 are included because said functional limitation would be an obvious properties of the referenced method. It is noted that the referenced method and the claimed method each used the same anti-CD3 antibody anti CD28 antibody attached to the beads to expand the population of T cells. When the prior art method is the same as a method described in the specification, it can be assumed the method will obviously perform the claimed process absent a showing of unobvious property.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-3, 11 and 12 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claims of the following copending applications: 20060121005, 20050226857, 20050214942, 20050153447, 20040241162, , 20030235908, 20030124122, 20030119185 , 20020119568, 20020058019 is evidenced by the disclosure of the instant specification on pages 81-83 for the same reasons set forth in the previous Office Action, mailed on 05/01/07.

While the instant and copending claims do differ in certain characteristics, the instant and copending claims appear to be drawn to the same or nearly the same method for selectively stimulating expanding of subpopulation of T cell from the mixed population comprising exposing said mixed population of T cells to a surface, wherein said surface has attached anti-Cd3 antibody- anti-CD28 antibody and wherein the ratio of surface:cells is high and then low.

As is evidenced by the disclosure of the instant specification on pages 81-83 , the exposure of a mixed population of T cells to high bead:cell ratio induces apoptosis in a portion of T cells population present in a mixed population of T cell.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments, filed 11/01/07 have been fully considered, but have not been found convincing.

Applicant asserts that he will considered filing a terminal disclaimer over the cited co-pending applications once the claims in the instant application are determined to be allowable.

It is noted that none of co-pending claims of the instant application are currently allowable.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference

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claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-3, 11 and 12 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17-21 of U.S. Patent No. 6867041 as is evidenced by the disclosure of the instant specification on pages 81-83 for the same reasons set forth in the previous Office Action, mailed on 11/02/06.

While the instant and claims 17-21 of U.S. Patent No. 6867041 do differ in certain characteristics, the instant and claims 17-21 of U.S. Patent No. 6867041 appear to be drawn to the same or nearly the same method for selectively stimulating expanding of subpopulation of T cell from the mixed population comprising exposing said mixed population of T cells to a surface, wherein said surface has attached anti-Cd3 antibody- anti-CD28 antibody and wherein the ratio of surface:cells is high and then low.

As is evidenced by the disclosure of the instant specification on pages 81-83, the exposure of a mixed population of T cells to high bead:cell ratio induces apoptosis in a portion of T cells population present in a mixed population of T cell.

Applicant's arguments, filed 11/01/07 have been fully considered, but have not been found convincing.

Applicant asserts that he will considered filing a terminal disclaimer over the cited co-pending applications once the claims in the instant application are determined to be allowable.

It is noted that none of co-pending claims of the instant application are currently allowable.



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8. No claim is allowed.

9. This is a RCE of applicant's earlier Application No.10/729,822 . All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is 571/ 272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571/ 272-0878 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michail A Belyavskiy/  
Primary Examiner, Art Unit 1644